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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,103	11/05/2001	A. James Mixson	5627*5	7244

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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,103	MIXSON, A. JAMES	
	Examiner	Art Unit	
	Scott D. Priebe, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-10,12-28,36-41 and 44* is/are allowed.

6)☒ Claim(s) *29-35,42,43 and 45-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claims 13-21 and 45-52 remain objected to because of the following informalities. These dependent claims either do not follow the independent claim from which they depend or are separated from the dependent claim from which they depend by a dependent claim that does not also depend from that same dependent claim (see MPEP § 608.01(n). Appropriate correction is required prior to allowance of the application. This correction may be made by examiner's amendment.

In the Reply of 3/6/06 Applicant has suggested the order be changed to 1-2, 45, 3-10, 46-48, 12, 22, 13-17, 49, 18-21, 23-27, 39, 28, 50, 29-30, 35, 52, 31-34, 36-38, 40-44, and 51. This order is acceptable.

Claim Rejections - 35 USC § 112

Claims 29-35, 42, 43, and 45-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite the limitation that at least 27% of the amino acids in the peptide are histidine. This limitation it not clearly supported by the original specification. The situation where claim 27 was amended to recite that the linear peptide contained at least 13 amino acids was supported by the specification showing a species of at least this length, and each other possible member of the range is an integral number, i.e. the range is discontinuous. However, the range of the fraction of amino acids that are histidine is a continuous range, and reflects not only a range of mole fraction of histidine but also a range of the length of the peptide. Applicant indicates that this limitation is supported by SEQ ID NO: 7. However, SEQ ID NO: 7 is 29 amino acids long, and the mole fraction of histidine in this particular peptide would not suggest to one of skill in the art that the inventors had contemplated a genus of peptide that shared one aspect of SEQ ID NO: 7, its mole fraction of histidine, but not other aspects, e.g. its length. Furthermore, the fraction of SEQ ID NO: 7 that is histidine is not 27%, but is approximately 27.586206896551724137931034482759%. Thus, SEQ ID NO: 7 would no more suggest a genus of at least about 27% histidine than it would suggest at least about 26%, 28% or 27.5%.

In claims 29 and 42, the above limitation is combined with an additional limitation that at least about 40% of the amino acids are amino acids with a net positive charge at physiological pH, e.g. Arg or Lys. This combination of limitations is not clearly supported by the original specification. Applicant indicates that this limitation is supported by combining the original disclosures at page 2, lines 20-23; page 12, line 31, to page 13, line 12; original claims 11 and 22; page 7, lines 13-18, and Figs. 8 and 9; page 27, lines 18-30; and page 29, lines 16-23, and Fig. 14. However, page 2, lines 20-23, describes the prior art, not what Applicant considered to be their invention. Pages 12-13 and original claims 11 and 12 support embodiments of the claimed invention where at

least 10% of the non-histidine amino acids are positively charged amino acids at physiological pH, not 40% of all amino acids are positively charged, and does not support or describe a genus where at least 27% of the amino acids are histidine, and along with page 7, lines 13-18, and Figs. 8 and 9; page 27, lines 18-30, merely support that the peptides may include amino acids that are positively charged at physiological pH, which is not the issue. At issue is whether the specification supports a genus of peptides where at least 27% of the amino acids are histidine and at least 40% are positively charged amino acids (at physiological pH). Page 29, lines 16-23, and Fig. 14, describe an experiment investigate the influence of histidine order, not percent, and polymer concentration on transfection. The two peptides to which Applicant refers were both 20-mers that were 60% His and 40% Lys, in different orders. This does not suggest the range that is now being claimed, but if anything suggests a genus of peptides that are 60:40::His:Lys. Applicant also points to pages 30-31 as support for branched peptides having at least 40% positively charged non-His amino acids. However, the mole fraction of the positively charged residues in these branched peptides is less than 40%, not at least 40%.

The convoluted reasoning advanced by Applicant raises doubt as to whether one of skill in the art would reach the newly claimed genus that Applicant suggests they would reach. There is no objective evidence of record that one of skill in the art would have arrived at this particular line of justification on one's own. Applicant is reminded that "Argument of counsel cannot take the place of evidence lacking in the record." *In re Scarbrough*, 182 USPQ 298, 302 (CCPA 1974).

In addition, the peptides upon which Applicant relies are linear. The claims embrace not only linear peptides, but also branched peptides. There is no support in the original specification

for branched peptides having these mole fractions of histidine and non-histidine positively charged amino acids. Attaching the cited peptides as side groups to a peptide backbone, e.g. oligolysine, would yield a different mole fraction of histidine (lower) or positively charged amino acid (higher, since Lys is used as the backbone) in the branched peptide than that present in the cited peptides.

Applicant's arguments filed 3/6/06 have been fully considered but they are not persuasive. Applicant does not dispute that there is no literal support for the "27%" limitation, either alone (e.g. claim 42) or in combination with the limitation of at least 40% non-His positively charged amino acids (e.g. claim 29). Applicant begins by speculating on what one of skill in the art would conclude concerning the minimum His content of the peptides in relation to their length. The length of SEQ ID NO: 7 was mentioned in the rejection as an example of one characteristic of SEQ ID NO: 7 that was omitted from the rejected generic claims. The rejection also points out the fact that this peptide is linear, whereas the rejected claims also embrace branched peptides, which also was omitted from the rejected generic claims. Other characteristics of SEQ ID NO: 7 that were omitted in crafting the rejected genus claims are the location and arrangement of the His residues, which are confined to the carboxy terminal half of the peptide alternating with Lys residues. By omitting these features, and focusing only on the His content of the peptide in drafting the rejected claims, Applicant has in essence indicated that a minimum His content of 27% is a critical or defining element of a genus, separate from other variables such as length, number and type of non-His residues, and the location and arrangement of the His and non-His residues. There is nothing in the original disclosure that explicitly or implicitly would lead one of skill in the art to a generic embodiment of the originally presented

invention wherein the His content of the linear or branched peptide is at least 27%. Applicant also points to page 29, lines 16-23, and Fig. 14, albeit not for support of the 27% limitation. This part of the specification points out the importance of the arrangement of the His and non-His residues in the peptide. This is another variable influencing the operability of the peptide of SEQ ID NO: 7 that was left out of drafting the rejected claims. Finally, it is not clear why one of skill in the art would use SEQ ID NO: 7 as an indication of implicitly disclosed genera at all. It is not described as being one of the preferred peptides; note its absence in the list on page 5, lines 12-22.

Applicant points to page 26, lines 1-9, and Fig. 3, where the specification explicitly teaches that the length of the peptide is an important variable with respect to enhancing transfection. Applicant then speculates that one of skill would also conclude that a transport polymer having at least 40% His content would enhance delivery. Applicant does not explain why one of skill would reach this conclusion. First, the 13-mer, which showed the least effect, is 38.5% His, i.e. less than 40% His. The specification notes that this peptide enhanced transfection. Also, the specification pointed out the importance of the length of the peptide here, not its His content. Finally, if, as Applicant reasons, one of skill would conclude from this experiment that the His content should be at least 40%, it argues against Applicant's position that the specification inherently teaches a range of at least 27%, which is substantially lower than 40%, up to 80% (claim 42) or up to 60% (claim 29).

Finally, applicant argues that the 27% limitation for branched peptides is supported simply because the specification teaches that the peptides can be branched or linear. In response, Applicant is missing the point here. SEQ ID NO: 7 is a linear peptide whose His content is about

27.6%. First, Applicant has not indicated where the original specification teaches including SEQ ID NO: 7 as a side chain in a branched polymer. Second, if this peptide were incorporated as a side chain into a branched peptide as taught in the specification for other peptides (see page 5, lines 12-22) include a backbone of non-His residues, e.g. one Lys or poly-Lys. Consequently, the mole fraction of His in the branched peptide would be lower than that of SEQ ID NO: 7. The only branched peptide with SEQ ID NO: 7 as a side chain that would have His content of at least 27% is where two peptides of SEQ ID NO: 7 are attached to a Lys residue (see Fig. 17) or other non-His backbone residue. Having two Lys residues in the backbone with three peptides of SEQ ID NO: 7 as side chains has a His content of less than 27%. With increasing length of the backbone, the His content drops further below 27%. Thus, it is not clear how the disclosure of SEQ ID NO: 7 would suggest that Applicant had contemplated a genus of branched peptides with a His content of at least 27%.

Applicant attempts to draw an analogy between this situation and the one reviewed by the court in *In re Wertheim*. In *Wertheim*, the only variable at issue was narrowing a disclosed range of 25%-60% to a claimed range of between 35% and 60%, with a disclosed embodiment of 36%. All numbers were integer values, and it is noted that between 35% and 60% does not include 35%, the lower limit is greater than 35%. The next integer value is 36%, which was the percentage used in the example. The situation here is substantially different. The original specification teaches that there are several important variables, including the length of the peptide, the percentages of His residues and non-His positively charged amino acid residues, the location and arrangement of the residues, and whether the peptide is linear or branched. The rejected generic claims are based on the value of only one of these variables possessed by the

peptide of SEQ ID NO: 7, and ignores the others.

The issues raised in Applicant's arguments are directed more to aspects of whether the specification enables the breadth of the claims than whether the originally filed disclosure supports the claimed genus based on a single characteristic of a single disclosed species, SEQ ID NO: 7. The disclosure of a broad genus and a species readable on that genus does not necessarily provide written description for an implicitly described subgenus that is embraced by the genus and comprises the species. *In re Smith*, 173 USPQ 679, 683 (CCPA 1972); *In re Lukach*, 169 USPQ 795, 797 (CCPA 1971). Disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. See *In re Shokal*, 113 USPQ 283 (CCPA 1957); *Purdue Pharma L.P. v. Faulding Inc.,* 56 USPQ2d 1481 (CAFC 2000). Taking one characteristic of an individual embodiment and making that characteristic the basis of a generic claim without further supporting disclosure is not in compliance with the written description requirement, see *Purdue Pharma* at 1487.

Double Patenting

The terminal disclaimer filed on 3/6/06 disclaiming the terminal portion of any patent granted on this application that would extend beyond the expiration date of a patent issuing from U.S. Application No. 10/131,909 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe

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